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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,622	08/25/1999	H. CRAIG DEES	PHO-107-DIV	5477

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EXAMINER

GABEL, GAILENE

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/382,622	Applicant(s) DEES ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on RCE and amendment filed 5/17/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,10,14,15,51,52,55-57,61,65,66 and 68 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 68 is/are allowed.
- 6) ☒ Claim(s) 1,4,10,15,51,52,55-57,61,65 and 66 is/are rejected.
- 7) ☒ Claim(s) 14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/24/05, 3/18/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on November 23, 2004 has been entered.

Amendment Entry

2. Applicant's amendment and response filed May 17, 2005 is acknowledged and has been entered. Claims 2, 3, 5-9, 16, 18-20, 50, 58-60, 62-64, and 67 have been cancelled. Claims 1, 4, 10, 51, 61, and 65 have been amended. Claim 68 has been added. Accordingly, claims 1, 4, 10, 14, 15, 51, 52, 55-57, 61, 65, 66, and 68 are pending and are under examination.

Rejections Moot or Withdrawn

3. The rejection of claims 2, 3, 5-9, 18-20, 50, 58-60, 62-64, and 67 are now moot in light of Applicant's cancellation of the claims.

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4. Rejections not reiterated herein have been withdrawn.

New Grounds of Rejection

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4, 10, 14, 15, 51, 52, 55-57, 61, 65, and 66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal or adequate descriptive support for the recitation of "said radiosensitizer agent does not include a liposome". This is a recitation of a negative limitation excluding liposomes from attachment to the radiosensitizer agent but the specification does not provide teaching or disclosure for the recitation of a negative limitation in the claims excluding liposomes. Specific guidance for the exclusion of a liposomes is not taught, the recitation of the negative limitation, "does not include a liposome" is therefore not supported or disclosed in the instant specification.

Since the limitation discussed supra lacks antecedent basis in the specification and does not flow from the teaching of Applicant's disclosure, and none of the originally

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filed claims recited the limitation in question, the claims are considered to constitute new matter. See *In re ANDERSON*, 176 USPQ 331 (CCPA 1973).

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

6. Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43, and 45-48 of copending ASN 09/799,785 in light of *Wihdholz et al.* (*Merck Index* (1983) published by Merck Co.). While claims 1, 26, 42, and 46 of ASN 09/799,785 recite that the medicament which is a radiosensitizer agent consists of "an aqueous solution of sodium, potassium, and lithium salt of a halogenated xanthene" whereas the rejected claims are silent with respect to such recitation, *Windholz et al.* specifically provide that it is an inherent property of halogenated xanthenes such as *Rose Bengal* to contain sodium, potassium, and lithium salts and halogenated xanthenes inherently exist in the form of sodium and potassium derivatives. Accordingly, this is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

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7. Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 are directed to the same invention as that of claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43, and 45-48 of commonly assigned ASN 09/799,785. The issue of priority under 35 U.S.C. 102(g) and possibly 35 U.S.C. 102(f) of this single invention must be resolved.

Since the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the assignee is required to state which entity is the prior inventor of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of monopoly.

Failure to comply with this requirement will result in a holding of abandonment of this application.

Obviousness Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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8. Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 12-14, 29, 32-34, 39, 40, and 46-49 of copending Application No. 09/817,448 in view of Heitz et al. (US Patent 4,846,789). Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims are drawn to a radiosensitizer agent for treatment of cancer tissue and tumors comprising of a halogenated xanthene which interacts with applied ionizing radiation to enhance therapeutic efficacy of the ionizing radiation.

ASN 09/817,448 differ from the instant invention in failing to teach that the halogenated xanthene is 4,5,6,7-tetrabromoerythrosin.

Heitz et al. disclose halogenated xanthene dyes, which are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation (see Abstract and Figure 5). According to Heitz et al., the halogenated xanthene dyes may absorb radiation at wavelengths outside of the visible spectrum including near infrared, and near to far ultraviolet spectrum (see column 3, lines 40-44). Heitz et al. teach that fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal are especially important (see column 4, lines 12-31). These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules or pellets for oral administration.

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It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute 4,5,6,7-tetrabromoerythrosin as taught by Heitz for the halogenated xanthene used with ionizing radiation as taught in ASN 09/817,448 because Heitz specifically taught that 4,5,6,7-tetrabromoerythrosin is an obvious variation of halogenated xanthenes known in the art.

In as far as the recitation of "the radiosensitizer agent does not include a liposome", it is an inherent property of radiosensitizer agents not to include liposomes, and that matter of factly, radiosensitizer agents have to be optionally derivatized to include a liposome. In the case of claims 1, 4-6, 12-14, 29, 32-34, 39, 40, and 46-49 of copending Application No. 09/817,448, the radiosensitizer agent has not been recited or taught to include liposomes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 10, 51, 52, 56, 57, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Heitz et al. (US Patent 4,846,789).

Heitz et al. disclose halogenated xanthene dyes, which are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation (see Abstract and Figure 5). According to Heitz et al., the halogenated xanthene dyes may absorb radiation at wavelengths outside of the visible spectrum including near infrared, and near to far ultraviolet spectrum (see column 3, lines 40-44). Heitz et al. teach that fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal are especially important (see column 4, lines 12-31). These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules, pellets, or salt blocks for oral administration.

In as far as the recitation of "the radiosensitizer agent does not include a liposome", it is an inherent property of halogenated xanthene dyes not to include liposomes, and that matter of factly, halogenated xanthene dyes have to be optionally derivatized to include a liposome. In the case of claims Heitz et al., the halogenated xanthene dyes have been taught to be included in capsules, pellets, and salt blocks.

With respect to the recitation of "activated using X-rays having an energy greater than 30 keV" in claim 10, "using radiosensitization or ionizing radiation, ... approximately greater than or equal to 1 keV and less than or equal to approximately 1000 MeV" in claims 51 and 52, "[interacting with ionizing radiation applied... which] comprises X-rays" in claim 56, and "X-rays have an energy between 30 kiloelectron volts and 1000 megaelectron volts" in claim 57, a recitation of the intended use of the

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claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

With respect to halogenated xanthenes such as 4,5,6,7-tetrabromoerythrosin being an imaging contrast agent, the discovery of a new property of an otherwise known compound or product such as 4,5,6,7-tetrabromoerythrosin, discovered to characteristically exist as an imaging contrast agent which is capable of enhancing efficacy of ionizing radiation applied to cancer or tumor in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. "derivatized 4,5,6,7-tetrabromoerythrosin by attachment to a biological targeting moiety", that is structurally different, novel, and nonobvious and different from all other commercially known halogenated xanthenes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4, 15, 55, 61, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heitz et al. (US Patent 4,846,789) in view of Williams et al. (US 5,576,013).

Heitz et al. has been discussed supra. Heitz et al. differ from the instant invention in failing to teach that the halogenated xanthene is attached to a biological targeting moiety.

Williams et al. disclose formulating halogenated xanthenes (photosensitizing agents) such as Rose Bengal with targeting moieties (penetrating solvents) in the form of a gel, lotion, cream, ointment which have hydrophilic or hydrophobic moieties to enhance targeting of the agent into affected tissue and to improve effectiveness of sensitization of the target tissue. The targeting moieties may include chelators, complexing agents, long/short hydrocarbons (xerogels, polyacrylic polymers (see column 5, line 6 to column 6, line 29).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate targeting moieties such as taught by Williams into halogenated xanthenes such as 4,5,6,7-tetrabromoerythrosin as taught by Heitz because Williams specifically taught that targeting moieties enhance targeting of the radiosensitizing agents into desired tissue to thus, improve effectiveness of sensitization of the target tissue. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate targeting moieties such as taught by Williams into radiosensitizing agents such as taught by Heitz in order to prevent problems such as failure of radiosensitizing agents to adhere to desired tissue properly and consequent reduction of effectiveness of treatment by sensitization as a result thereof.

Response to Arguments

11. Applicant's arguments filed May 17, 2005 have been considered but are moot in view of the new grounds of rejection.

Allowable Subject Matter

12. Claim 68 is allowed. Prior art of record fails to teach or fairly suggest a radiosensitizer agent comprising a halogenated xanthene that is specifically attached to a biological targeting moiety to enhance targeting of the halogenated xanthene to desired cancer or tumor tissue.

13. Claim 14 is objected to as being dependent from a rejected base claim.

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Correspondence

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
July 5, 2005

